

WHAT IS CLAIMED IS:

1. A large circular nucleic acid molecule comprising a target-specific antisense region, which specifically binds to a portion of RNA expressed from a gene, wherein
5 said antisense molecule is effective for reducing the expression of said gene.
2. The large circular nucleic acid molecule according to claim 1, wherein said molecule is at least about 3,000 nucleotides long.
- 10 3. The large circular nucleic acid molecule according to claim 1, wherein said antisense region of the molecule is at least about 50 nucleotides long.
4. The large circular nucleic acid molecule according to claim 1, wherein said antisense region is substantially complementary to an entire gene sequence.
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5. The large circular nucleic acid molecule according to claim 1, wherein said nucleic acid molecule is a single stranded form of a recombinant bacteriophage or phagemid genome.
- 20 6. The large circular nucleic acid molecule according to claim 5, wherein said bacteriophage or phagemid is derived from a filamentous phage.
7. The large circular nucleic acid molecule according to claim 6, wherein said filamentous phage is phage M13.
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8. A recombinant vector comprising the large circular nucleic acid molecule according to claim 1.
9. The vector according to claim 8, wherein said vector is derived from a
30 filamentous phage.

10. A host cell comprising the vector according to claim 8.

11. A composition comprising a large circular nucleic acid molecule comprising a target-specific antisense region, which specifically binds to a portion of RNA expressed from a gene, wherein said antisense molecule is effective for reducing the expression of said gene, and a pharmaceutically acceptable carrier thereof.

12. A method for inhibiting expression of a selected protein by a large circular nucleic acid molecule targeted to an RNA encoding the selected protein comprising, targeting the nucleic acid molecule to the RNA such that the nucleic acid molecule hybridizes with the RNA to form a duplex with the RNA, wherein the duplex inhibits expression of the selected protein.

13. The method according to claim 12, wherein expression of said target protein causes cell proliferation or cancer.

14. The method according to claim 13, wherein said cancer is leukemia, lung cancer, liver cancer, colon cancer, stomach cancer, pancreatic cancer, brain cancer or prostate malignancy.

15. The method according to claim 14, wherein said cancer is leukemia, cervical cancer, or breast cancer.

16. The method according to claim 13, wherein said target protein is tumor necrosis factor, nuclear factor, MYB, MYC, RAS, or cell division kinase.

17. The method according to claim 12, wherein said protein is a viral protein.

18. The method according to claim 17, wherein said virus is herpes, human papilloma virus (HPV), HIV, small pox, mononucleosis (Epstein-Barr virus), hepatitis, or respiratory syncytial virus (RSV).

19. The method according to claim 12, wherein expression of said target protein causes a metabolic disease or an immunological disorder.

5 20. The method according to claim 19, wherein said metabolic disease is phenylketonuria (PKU), primary hypothyroidism, galactosemia, abnormal hemoglobins, types I and II diabetes, or obesity.

21. The method according to claim 18, wherein said immunological disorder is
10 Sjogren's Syndrome, antiphospholipid syndrome, immune complex diseases, Purpura, Schoenlein-Henoch, immunologic deficiency syndromes, systemic lupus erythematosus, immunodeficiency, rheumatism, kidney, or liver sclerosis.

22. A chimeric large circular nucleic acid molecule comprising target-specific
15 antisense regions, which specifically bind to a plurality of target RNA expressed from a plurality of target genes, wherein said nucleic acid molecule is effective for reducing the expression of said genes.

23. A composition comprising a chimeric large circular nucleic acid molecule
20 comprising target-specific antisense regions, which specifically bind to a plurality of target RNA expressed from a plurality of target genes, wherein said nucleic acid molecule is effective for reducing the expression of said genes, and a pharmaceutically acceptable carrier thereof.

25 24. A method for inhibiting expression of a plurality of selected proteins by a large circular nucleic acid molecule targeted to a plurality of RNA molecules encoding a plurality of selected proteins comprising,

(i) generating a chimeric large circular nucleic acid molecule comprising target-specific antisense regions targeted to said plurality of target RNA; and

30 (ii) targeting the plurality of RNA such that the chimeric large circular nucleic acid molecule hybridizes with said RNA to form a duplex, wherein the duplex reduces

expression of the plurality of selected proteins.

25. A method for inhibiting cell proliferation, comprising,
administering to said cell, a large circular nucleic acid molecule that comprises
5 one or more antisense region substantially complementary to one or more target gene,
in which inhibiting expression of said gene or genes inhibits cell proliferation.

26. A method of making a large circular nucleic acid molecule comprising target-
specific antisense region which inhibits expression of a selected protein, comprising,
10 (i) inserting a target-specific DNA of interest into a phage or phagemid genome;
(ii) allowing the phage to generate a single stranded form, which is the large
circular nucleic acid molecule; and
(iii) isolating said large circular nucleic acid molecule by gel filtration column.

15 27. A method of screening for a function of a gene comprising,
(a) generating a large circular nucleic acid molecule comprising an antisense
region that is substantially complementary to an RNA expressed from a cell;
(b) contacting a cell with the large circular nucleic acid molecule such that the
antisense molecule enters the cell and hybridizes to an RNA expressed in the cell to
20 inhibit expression of its gene product; and
(c) assaying the cell for a variation of a phenotype.

28. The method according to claim 27, wherein steps (a) to (c) are applied to a
library of said large circular nucleic acid molecule.

25 29. The method according to claim 27, wherein said nucleic acid molecule is a
single stranded form of a recombinant bacteriophage or phagemid genome.

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